doi: 10.13241/j.cnki.pmb.2017.16.036

普罗卡因联合头孢曲松治疗急性胰腺炎的临床疗效研究 *

杨立安[1] 张震波[1] 冯 伟[1] 杨福泉[1] 胡 帅[2]

（1 陕西省第二人民医院 肝胆普外科 陕西 西安 710005；2 第四军医大学第一附属医院西京医院 产科 陕西 西安 710032）

摘要 目的：探讨普罗卡因联合头孢曲松对急性胰腺炎患者临床疗效及肠粘膜屏障功能的影响。**方法：**选择 2013 年 8 月至 2016 年 8 月我院接诊的 92 例急性胰腺炎患者，通过随机数表法分为观察组（n=46）和对照组（n=46）。对照组使用头孢曲松钠治疗，观察组在对照组基础上联用普罗卡因。比较两组临床症状缓解时间、治疗前后血清肿瘤坏死因子（TNF-α）、白介素（IL）-6、超敏 C 反应蛋白（hs-CRP）、降钙素原和 D- 乳酸水平及临床疗效。**结果：**观察组腹痛缓解时间、腹胀缓解时间、禁食时间、血清淀粉酶恢复正常时间均比对照组短（P＜0.05）；治疗后，观察组血清 TNF-α、IL-6、hs-CRP、降钙素原、D- 乳酸水平均显著低于对照组（P＜0.05），总有效率明显高于对照组（P＜0.05）。**结论：**普罗卡因联合头孢曲松可有效缓解急性胰腺炎患者的临床症状，降低机体炎性反应，促进肠粘膜屏障功能的恢复。

关键词：急性胰腺炎；头孢曲松；普罗卡因；降钙素原；D- 乳酸

中图分类号：R576 **文献标识码：**A **文章编号：**1673-6273(2017)16-3140-04

Curative Efficacy of Procaine Combined with Cefatriaxone in Treatment of Acute Pancreatitis*

YANG Li-an[1], ZHANG Zhen-bo[1], FENG Wei[1], YANG Fu-quan[1], HU Shuai[2]

(1 Department of general surgery, the second people's Hospital of Shaanxi Province, Xi'an, Shaanxi, 710005, China; 2 Department of Obstetrics, the First Affiliated Hospital of The Fourth Military Medical University, Xijing Hospital, Xi'an, Shaanxi, 710032, China)

ABSTRACT Objective: To study the curative efficacy of procaine combined with cefatriaxone in treatment of acute pancreatitis and its effects on serum levels of procalcitonin and D-Lactate. **Methods:** 92 patients with acute pancreatitis who were treated in our hospital from August 2013 to August 2016 were selected and randomly divided into the control group (n=46) and the observation group (n=46). The patients in the control group were treated with cefatriaxone, while the patients in the observation group were treated with the procaine on the basis of the control group. Then the remission time of clinical symptoms, and the serum levels of the tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), high sensitive C reactive protein (hs-CRP), procalcitonin and D-Lactate, and the clinical efficacy of the two groups were observed and compared before and after the treatment. **Results:** The relief time of abdominal pain and distension, the fasting time, and the recovery of serum amylase in the observation group were shorter than those of the control group (P<0.05); The serum levels of tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), high sensitive C reactive protein (hs-CRP) and D-Lactate of the observation group were lower than those of the control group (P<0.05); The total effective rate of the observation group was significantly higher than that of the control group (P<0.05). **Conclusion:** Procaine combined with cefatriaxon has better clinical effect on the treatment of acute pancreatitis, which can effectively alleviate the clinical symptoms, reduce the serum levels of inflammatory response, and promote the recovery of intestinal mucosal barrier functions, and it's worthy of clinical application.

Key words: Acute pancreatitis; Cefatriaxone; Procaine; Procalcitonin; D-Lactate

Chinese Library Classification(CLC): R576 Document code: A

Article ID:1673-6273(2017)16-3140-04

前言

急性胰腺炎是临床常见的急腹症，症状主要表现为腹痛、腹胀、恶心呕吐、血清淀粉酶增加等，常会累及多个脏器，若得不到及时的治疗，可能会致使患者发生多器官功能衰竭，严重的会引发死亡[1,2]。研究显示急性胰腺炎患者肠粘膜屏障功能多伴有不同程度的损伤，而保护肠粘膜功能为该病的治疗提供了另一种途径[3]。目前，临床上对于该病的治疗主要在常规胃肠减压、禁食、维持水电解质平衡、营养支持等基础上，再加以药物的联合治疗，但疗效不一，仍需进行深入的探讨[4,5]。本研究主要观察了普罗卡因联合头孢曲松治疗急性胰腺炎的临床疗效及其对患者肠粘膜屏障功能的影响，现报道如下。

1 资料与方法

1.1 一般资料

选择 2013 年 8 月至 2016 年 8 月我院接诊的 92 例急性胰

* 基金项目：陕西省自然科学基金项目(2009FJ6053）

作者简介：杨立安(1975-)，男，本科，主治医师，研究方向：肝胆普外科疾病的诊治与研究，电话：13991289592

(收稿日期：2016-11-03 接受日期：2016-11-16)

腺炎患者。纳入标准:① 符合急性胰腺炎诊断标准[6],并通过体格检查、血生化指标检测得以确诊;② 对本次研究所使用药物无过敏史;③ 同意参与此次研究。排除标准:① 由于手术、外伤所致的胰腺炎;② 存在免疫、代谢性疾病,伴有恶性肿瘤,肝肾功能严重不全者;③ 研究前 1 月内有消化酶抑制剂、生长抑素等类似药物应用史;④ 伴有严重病原微生物感染。通过随机数表法分为观察组和对照组,各 46 例。观察组男 26 例,女 20 例,年龄 25~64 岁,平均(43.85± 3.01)岁,病程 0.5~3.5d,平均(2.13± 0.21)d,其中 40 例轻型胰腺炎,6 例重型胰腺炎;对照组男 25 例,女 21 例,年龄 27~65 岁,平均(44.02± 2.94)岁,病程 0.5~4.0d,平均(2.15± 0.18)d,39 例轻型胰腺炎,7 例重型胰腺炎。本次研究在我院伦理委员会批准下实施,两组患者在性别、年龄、病程、病情严重程度无显著差异(P>0.05),具有可比性。

1.2 治疗方法

两组患者均给予常规抗炎、胃肠减压、禁食、止痛、抗痉挛、抑制胃酸分泌、维持水电解质平衡、营养支持等处理。对照组给予头孢曲松钠(规格 2.0 g,批号 130712,厂家:西南药业股份有限公司)静脉注射,0.5~1 g/ 次,12 h/ 次。观察组在对照组基础上加用 1%普罗卡因(规格 20 mL: 0.1 g,批号 130725,厂家:上海旭东海普药业有限公司)静脉滴注 100 mL,1 d/ 次。两组患者均连续治疗 5 d。

1.3 观察指标

① 记录临床指标缓解时间,包括腹痛缓解时间、腹胀缓解时间、禁食时间、血清淀粉酶恢复正常时间;② 治疗前后抽取患者空腹静脉血 3ml,检测炎性因子:肿瘤坏死因子(TNF-α)、白介素(IL)-6、超敏 C 反应蛋白(hs-CRP)以及肠粘膜屏障功能指标:降钙素原、D 乳酸;检测方式均使用上海恒远生物科技有限公司所生产的 ELISA 试剂盒。

1.4 疗效评定标准[7]

显效:治疗后腹痛、腹胀等临床体征得到完全缓解,检测血、尿淀粉酶水平恢复到正常水平;有效:治疗后临床症状体征得到一定,检测血、尿淀粉酶水平得到一定改善;无效:治疗后好转程度未达到以上标准。

1.5 统计学分析

数据用 SPSS18.0 软件包进行处理,计量资料用均数± 标准差($\bar{x}\pm s$)表示,并采用 t 检验,计数资料的比较采用 x^2 检验,等级资料的比较采用秩和检验,P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组患者临床指标的缓解时间比较

观察组腹痛缓解时间、腹胀缓解时间、禁食时间、血清淀粉酶恢复正常时间均比对照组短(P<0.05),见表 1。

表 1 两组患者临床指标缓解时间($\bar{x}\pm s$, d)

Table 1 Comparison of the remission time of clinical indexes between two groups($\bar{x}\pm s$, d)

Groups	n	Abdominal pain	Abdominal distension	Fasting time	Serum amylase recovery
Observation group	46	3.41± 0.43	3.34± 0.37	5.48± 0.71	3.05± 0.47
Control group	46	4.20± 0.51	4.98± 0.72	7.32± 1.14	4.31± 0.53
t value		8.032	13.740	9.292	12.064
P value		0.000	0.000	0.000	0.000

2.2 两组患者治疗前后血清炎性因子水平的比较

治疗前,两组患者在各炎性因子水平比较均无显著差异(P>0.05)。治疗后,两组患者血清 TNF-α、IL-6 和 hs-CRP 水平均较治疗前显著降低(P<0.05),且观察组以上指标均明显低于对照组(P<0.05),见表 2。

表 2 两组患者治疗前后血清炎性因子水平比较($\bar{x}\pm s$)

Table 2 Comparison of the serum levels of inflammatory factors between two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	TNF-α(ng/L)		IL-6 ng/L)		hs-CRP(mg/L)	
		Before treatment	Before treatment	Before treatment	Before treatment	Before treatment	Before treatment
Observation group	46	84.31± 10.45	31.34± 5.31*	335.06± 20.18	102.12± 14.51*	23.41± 5.62	6.92± 1.05*
Control group	46	84.46± 10.26	53.40± 7.94*	334.89± 20.75	138.96± 16.43*	23.49± 5.56	9.53± 1.47*
t value		0.069	15.664	0.040	11.399	0.067	9.799
P value		0.945	0.000	0.968	0.000	0.945	0.000

Note: Compared with the same group before treatment,*P<0.05.

2.3 两组患者治疗前后肠粘膜屏障功能比较

治疗前,两组患者肠道粘膜屏障功能指标无显著差异(P>0.05)。治疗后,两组患者血清降钙素原、D- 乳酸水平均较治疗前显著降低(P<0.05),且观察组以上指标均比对照组低(P<0.05),见表 3。

2.4 两组患者临床疗效比较

观察组总有效率为 95.65%,显著高于对照组(76.08%,P<0.05),见表 4。

表 3 两组患者治疗前后肠粘膜屏障功能比较($\bar{x}\pm s$)

Table 3 Comparison of the intestinal mucosal barrier functions before and after treatment between two groups($\bar{x}\pm s$)

Groups	n	Procalcitonin(ng/mL)		D-lactate(mg/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	46	5.48± 1.14	2.15± 0.36*	12.74± 3.42	6.23± 1.06*
Control group	46	5.52± 1.11	3.48± 0.48*	12.71± 3.26	9.58± 1.15*
t value		0.170	15.034	0.043	14.527
P value		0.865	0.000	0.966	0.000

Note: Compared with the same group before treatment,*P＜0.05.

表 4 两组患者临床疗效比较(例,%)

Table 4 Comparison of the clinical efficacy between two groups(n, %)

Group	n	Markedly effectiv	Effective	Invalid	Total effective rate
Observation group	46	24(52.17)	20(43.48)	2(4.35)	44(95.65)
Control group	46	17(36.96)	18(39.13)	11(23.91)	35(76.08)
P value					P=0.007

3 讨论

急性胰腺炎主要表现为胰腺组织出血、自身水肿,严重的甚至发生胰腺组织细胞坏死的炎性反应。随着目前人们生活饮食的不断改变,酒精类饮料的增加,致使发病率日趋增加,给患者及其家属带来较大的负担[8]。在急性胰腺炎患者的常规治疗中,应用抗生素是种常见的手段[9,10]。头孢曲松作为第三代头孢菌素类抗生素,可应用于包括下呼吸道感染、尿路感染、腹腔感染、盆腔感染、骨和关节感染、手术期感染的预防[11],但单独应用抗生素在急性胰腺炎患者中效果不够理想。普罗卡因是一种局部麻醉剂,对注射部位组织会产生局部扩血管效果,在各类疾病中也存在着较为广泛的应用[12]。有研究指出其可解除患者小叶内动脉括约肌痉挛以及胰腺的微循环,隔断水肿性胰腺炎向坏死性的发展,从而达到治疗效果[13]。其作用机制为包括以下几个方面:① 作为一种钙离子非选择性抑制剂,抑制微循环内皮细胞的超级化,保护细胞膜的稳定性,增加前列环素,进一步保护组织微循环;② 使腹腔淋巴液回流增加,消除炎症所造成的水肿,从而改善机体微循环;③ 抑制胰酶 A 的活性,降低胰腺组织的自身消化[14]。但目前临床上对于普罗卡因联合头孢曲松的治疗方案较少,本次研究结果显示与单用头孢曲松治疗的患者比较,联合普罗卡因治疗的患者,腹痛、腹胀缓解时间,禁食、血清淀粉酶恢复时间均较短,且所达到的总有效率高达95.65%,比单独用药更具有优势。

在急性胰腺炎的发生发展过程中,白细胞过度激活 - 炎性因子级联瀑布效应发挥了重要的作用,其中研究较多的炎性因子包括 TNF-α、IL-6、hs-CRP,其表达水平在急性胰腺炎患者中呈明显升高,参与了上调中性粒细胞功能,对炎性介质转录调节、增加血管通透性等多种病理过程,致使胰腺及其周围组织发生损伤,促进疾病发展[15,16]。因此,消除急性胰腺炎患者体内炎性反应具有积极意义。本研究结果显示:相比于单独使用头孢曲松,联合应用普罗卡因的患者血清 TNF-α、IL-6、hs-CRP 水平下降更为明显,提示表明联合用药可通过不同机制发挥其抑制炎性反应的作用,从而提高治疗效果。

在炎性反应、内毒素、肠道微循环障碍等因素的影响下,急性胰腺炎患者的肠粘膜功能存在着损伤,从而加重感染,促进疾病感染[17,18]。当肠道粘膜屏障功能发生损伤时,容易致使患者出现肠源性内毒素血症, 刺激降钙素原、D- 乳酸的过度释放,增加水平表达,可对肠粘膜屏障功能进行间接性的反应[19,20]。本次研究结果显示两种方式治疗的患者降钙素原、D- 乳酸均得到了不同程度的下降,但联合用药的患者效果更为显著,显示出联合方案在保护患者肠粘膜屏障功能上优势更加明显,这也可能是提高急性胰腺炎患者治疗效果的一个作用机制,联合普罗卡因的应用可改善胰腺的微循环, 降低胰腺组织的自身消化,从而促进肠粘膜屏障功能的恢复。

综上所述,普罗卡因联合头孢曲松可有效缓解急性胰腺炎的临床症状,降低机体炎性反应,促进肠粘膜屏障功能的恢复。

参 考 文 献(References)

[1] Avanesov M, Weinrich JM, Kraus T, et al. MDCT of acute pancreatitis: Intraindividual comparison of single-phase versus dual-phase MDCT for initial assessment of acute pancreatitis using different CT scoring systems[J]. Eur J Radiol, 2016, 85(11): 2014-2022

[2] Selfa Muñoz A, Calzado Baeza SF, Palomeque Jimé nez A, et al. Acute pancreatitis associated with the intragastric balloon [J]. Gastroenterol Hepatol, 2016, 39(9): 603-604

[3] Qin DP, Wei X, Fang GD, et al. Intervention Effect of Modified Dachengqi Decoction on Intestinal Mucosal Barrier of Severe Acute Pancreatitis Model Rats [J]. Zhongguo Zhong Xi Yi Jie He Za Zhi, 2015, 35(12): 1482-1489

[4] Dick JF, Gardner TB, Merrens EJ. Acute pancreatitis: New developments and strategies for the hospitalist [J]. J Hosp Med, 2016, 11(10): 724-729

[5] Wei AL, Guo Q, Wang MJ, et al. Early complications after interventions in patients with acute pancreatitis [J]. World J

Gastroenterol, 2016, 22(9): 2828-2836

[6] Department of pancreatic surgery, Chinese Medical Association. Guidelines for the diagnosis and treatment of acute pancreatitis(2014) [J]. Chin J Pract Surg, 2015, 35(01): 4-7

[7] Zhao Y, Li YX, Lin J, et al. Effect of octreotide combined with lactulose enema on inflammatory cytokines and intestinal mucosal barrier in acute pancreatitis [J]. Chinese Journal of Biochemical Pharmaceutics, 2016, 36(05): 110-113

[8] Kochar NS, Sehgal B, Solomon L. Acute pancreatitis and Myocarditis: A rare complication of acute hepatitis E infection [J]. J Assoc Physicians India, 2016, 64(1): 111

[9] Baltatzis M, Jegatheeswaran S, O'Reilly DA, et al. Antibiotic use in acute pancreatitis: Global overview of compliance with international guidelines[J]. Pancreatology, 2016, 16(2): 189-193

[10] Huber W, Kemnitz V, Phillip V, et al. Outcome prediction, fluid resuscitation, pain management, and antibiotic prophylaxis in severe acute pancreatitis[J]. Intensive Care Med, 2015, 41(11): 2034-2035

[11] Murata S, Aomatsu T, Yoden A, et al. Fasting and bed rest, even for a relatively short period, are risk factors for ceftriaxone-associated pseudolitiasis[J]. Pediatr Int, 2015, 57(5): 942-946

[12] Wang ZH, Ouyang BS, Chen Y, et al. Chloroprocaine combined with morphine epidural anesthesia on analgesia after cesarean section[J]. The Journal of Clinical Anesthesiology, 2015, 31(08): 810-811

[13] Chen XY. The use of procaine in clinic [J]. Contemporary medicine, 2014, 12(15): 155-156

[14] Wilms B, Meffert KS, Schultes B. Procaine infusion for pain treatment of acute pancreatitis: a randomized, placebo-controlled double-blind trial[J]. Dtsch Med Wochenschr, 2010, 135(46): 2290-2295

[15] Wang LZ, Luo MY, Zhang JS, et al. Effect of ulinastatin on serum inflammatory factors in Asian patients with acute pancreatitis before and after treatment: a meta-analysis [J]. Int J Clin Pharmacol Ther, 2016, 54(11): 890-898

[16] Karpavicius A, Dambrauskas Z, Gradauskas A, et al. The clinical value of adipokines in predicting the severity and outcome of acute pancreatitis[J]. BMC Gastroenterol, 2016, 16(1): 99

[17] Li Y, Wu H, Deng Y, et al. Changes of Intestinal Mucosal Barrier and Intestinal Flora in Rats with Severe Acute Pancreatitis [J]. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi, 2015, 32(2): 412-417

[18] Yao P, Cui M, Li Y, et al. Effects of rhubarb on intestinal flora and toll-like receptors of intestinal mucosa in rats with severe acute pancreatitis[J]. Pancreas, 2015, 44(5): 799-804

[19] Tu XH, Huang SX, Li WS, et al. Mesenchymal stem cells improve intestinal integrity during severe acute pancreatitis [J]. Mol Med Rep, 2014, 10(4): 1813-1820

[20] Liang HY, Chen T, Yan HT, et al. Berberine ameliorates severe acute pancreatitis induced intestinal barrier dysfunction via a myosin light chain phosphorylation dependent pathway [J]. Mol Med Rep, 2014, 9(5): 1827-1833

(上接第 3090 页)

[22] 曲同庆. 激素联合丙种球蛋白治疗吉兰-巴雷综合征的疗效观察[J]. 中国实用神经疾病杂志, 2014, (04): 23-25
Qu Tong-qing. Curative efficacy observation of corticosteroids combination IVIG treating Guillain-Barré syndrome [J]. Chinese practical neurological diseases journal, 2014, (04): 23-25

[23] R Van Koningsveld P I M S. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barré syndrome: randomised trial [J]. Lancet, 2004, (363): 192-196

[24] Susuki K Y N. Effect of methylprednisolone in patients with Guillain-Barré syndrome[J]. Lancet, 2004, (363): 1236-1237